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A Disease Concept Model and a Natural History Study of SLC6A1-NDD

Marie Varnet, MD

Children's Hospital Colorado
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Affiliated with
Department of Pediatrics
SCHOOL OF MEDICINE
UNIVERSITY OF COLORADO **ANSCHUTZ MEDICAL CAMPUS**

Disease Concept Model

- Disease concept models (DCM) are frameworks built by engaging the community to understand the drivers of symptom burden. A DCM seeks to:
  - Identify the major symptom domains according to caregivers
  - Demonstrate what areas of life are most affected by symptom burden in both caregivers and the individuals

Previous DCM's

Taking the lead from from those who came before

- Built a framework for putting the lived experience first, not just what could be easily quantified

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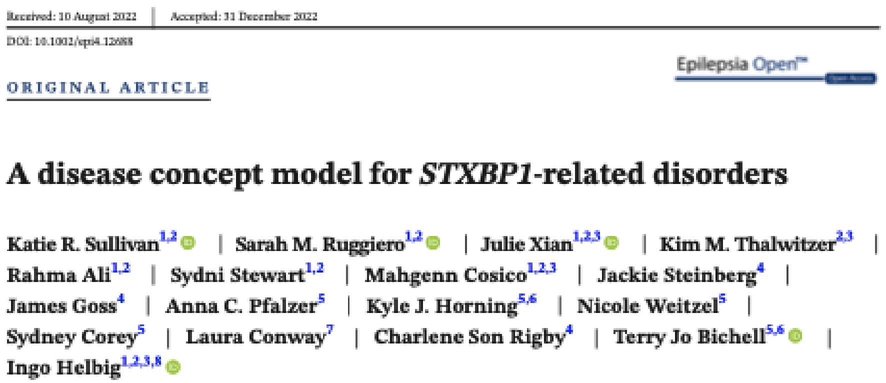
ORIGINAL ARTICLE

Measuring What Matters to Individuals with Angelman Syndrome and Their Families: Development of a Patient-Centered Disease Concept Model

Tom Willgoss[1] · Daiana Cassater[2] · Siobhan Connor[1] · Michelle L. Krishnan[2] · Meghan T. Miller[2] · Carla Dias-Barbosa[3] · Dawn Phillips[4] · Julie McCormack[5] · Lynne M. Bird[6] · Rebecca D. Burdine[7] · Sharon Claridge[8] · Terry Jo Bichell[9]



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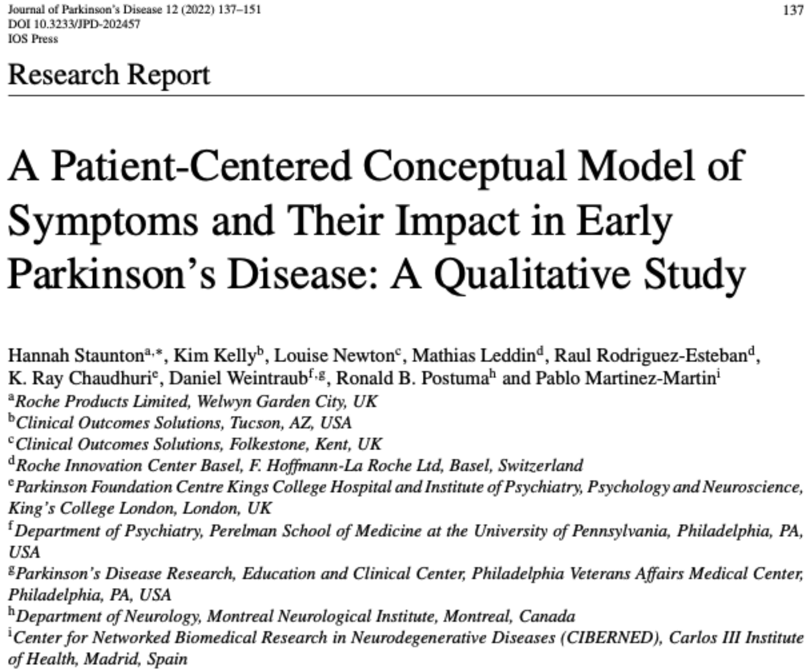
Epilepsia Open™

ORIGINAL ARTICLE

A disease concept model for *STXBP1*-related disorders

Katie R. Sullivan[1,2] | Sarah M. Ruggiero[1,2] | Julie Xian[1,2,3] | Kim M. Thalwitzer[2,3] | Rahma Ali[1,2] | Sydni Stewart[1,2] | Mahgenn Cosico[1,2,3] | Jackie Steinberg[4] | James Goss[4] | Anna C. Pfalzer[5] | Kyle J. Horning[5,6] | Nicole Weitzel[5] | Sydney Corey[5] | Laura Conway[7] | Charlene Son Rigby[4] | Terry Jo Bichell[5,6] | Ingo Helbig[1,2,3,8]



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IOS Press

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Research Report

A Patient-Centered Conceptual Model of Symptoms and Their Impact in Early Parkinson's Disease: A Qualitative Study

Hannah Staunton[a,*], Kim Kelly[b], Louise Newton[c], Mathias Leddin[d], Raul Rodriguez-Esteban[d], K. Ray Chaudhuri[e], Daniel Weintraub[f,g], Ronald B. Postuma[h] and Pablo Martinez-Martin[i]
[a] *Roche Products Limited, Welwyn Garden City, UK*
[b] *Clinical Outcomes Solutions, Tucson, AZ, USA*
[c] *Clinical Outcomes Solutions, Folkestone, Kent, UK*
[d] *Roche Innovation Center Basel, F. Hoffmann-La Roche Ltd, Basel, Switzerland*
[e] *Parkinson Foundation Centre Kings College Hospital and Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK*
[f] *Department of Psychiatry, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, USA*
[g] *Parkinson's Disease Research, Education and Clinical Center, Philadelphia Veterans Affairs Medical Center, Philadelphia, PA, USA*
[h] *Department of Neurology, Montreal Neurological Institute, Montreal, Canada*
[i] *Center for Networked Biomedical Research in Neurodegenerative Diseases (CIBERNED), Carlos III Institute of Health, Madrid, Spain*

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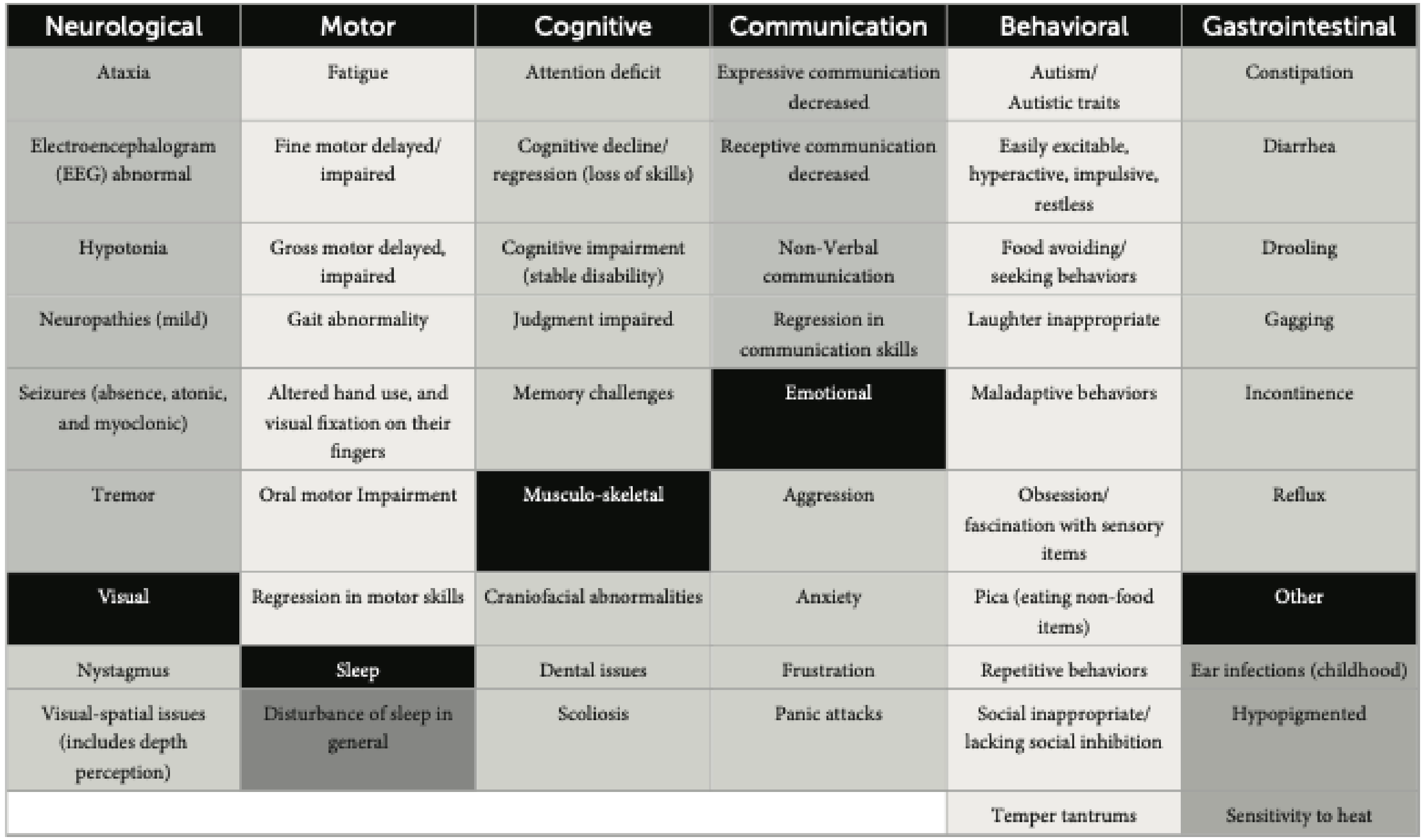
A draft conceptual model of SLC6A1 neurodevelopmental disorder

Kimberly Goodspeed[1]*, Lindsay R. Mosca[2],
Nicole C. Weitzel[2], Kyle Horning[3], Elijah W. Simon[2],
Anna C. Pfalzer[3], Maya Xia[3], Katherine Langer[2],
Amber Freed[4], Megan Bone[1], Maria Picone[5] and
Terry Jo V. Bichell[3]*

- Focused on conversations between families of people with SLC6A1-NDD on social media
- Allowed for analysis of spontaneous conversations, what caregivers will ask about or discuss when not in a medical setting

TABLE 1 Draft disease concept map for SLC6A1 neurodevelopmental disorder (SLC6A1-NDD).



Neurological	Motor	Cognitive	Communication	Behavioral	Gastrointestinal
Ataxia	Fatigue	Attention deficit	Expressive communication decreased	Autism/ Autistic traits	Constipation
Electroencephalogram (EEG) abnormal	Fine motor delayed/ impaired	Cognitive decline/ regression (loss of skills)	Receptive communication decreased	Easily excitable, hyperactive, impulsive, restless	Diarrhea
Hypotonia	Gross motor delayed, impaired	Cognitive impairment (stable disability)	Non-Verbal communication	Food avoiding/ seeking behaviors	Drooling
Neuropathies (mild)	Gait abnormality	Judgment impaired	Regression in communication skills	Laughter inappropriate	Gagging
Seizures (absence, atonic, and myoclonic)	Altered hand use, and visual fixation on their fingers	Memory challenges	**Emotional**	Maladaptive behaviors	Incontinence
Tremor	Oral motor Impairment	**Musculo-skeletal**	Aggression	Obsession/ fascination with sensory items	Reflux
Visual	Regression in motor skills	Craniofacial abnormalities	Anxiety	Pica (eating non-food items)	**Other**
Nystagmus	**Sleep**	Dental issues	Frustration	Repetitive behaviors	Ear infections (childhood)
Visual-spatial issues (includes depth perception)	Disturbance of sleep in general	Scoliosis	Panic attacks	Social inappropriate/ lacking social inhibition	Hypopigmented
				Temper tantrums	Sensitivity to heat

Methods

Semi-structured interviews were conducted with caregivers and providers (physicians, therapists) of individuals with SLC6A1-NDD.

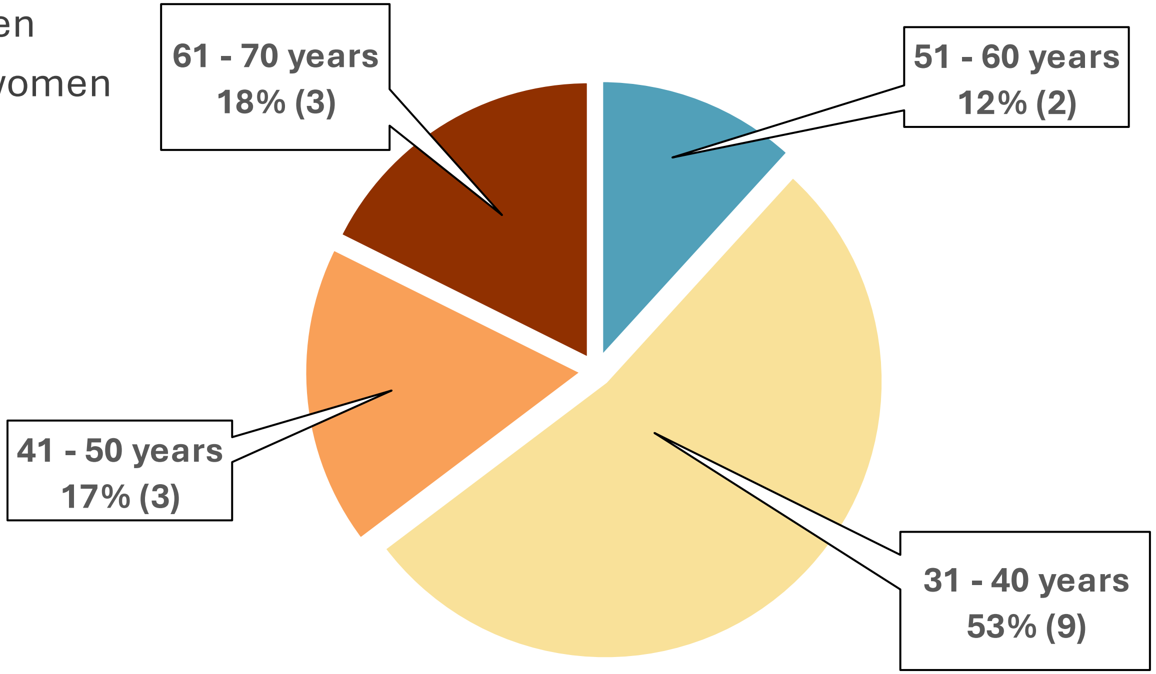
- **Participants were recruited through the UTSW natural history study and patient advocacy group, SLC6A1 Connect.**
- **Hour-long interviews were recorded, transcripts anonymized, then independently coded using Dedoose software by paired teams.**
- **There are 547 individual codes available, our teams applied 13,055 codes**
- **Unless otherwise stated, code counts were normalized by co-code application per transcript to account for unconscious bias in interview and coding styles.**
- **Co-codes indicate the topics are related by the caregiver’s narrative; that they were discussed within the same part of the interview.**

Participants

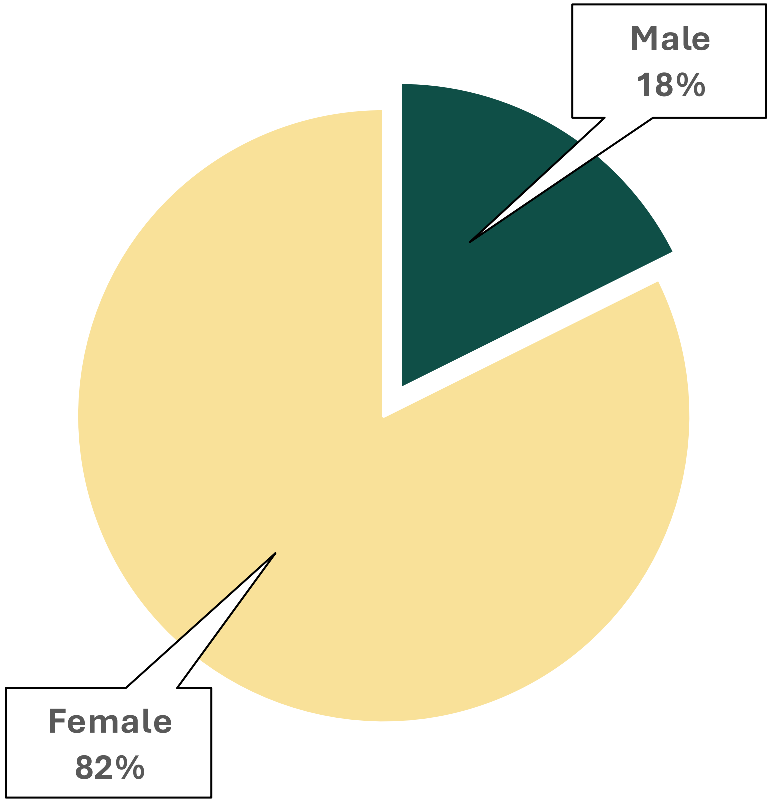
Caregiver Participants

- A total of 17 caregiver interviews:

  3 men
  14 women



Caregiver Age at the time of Interview



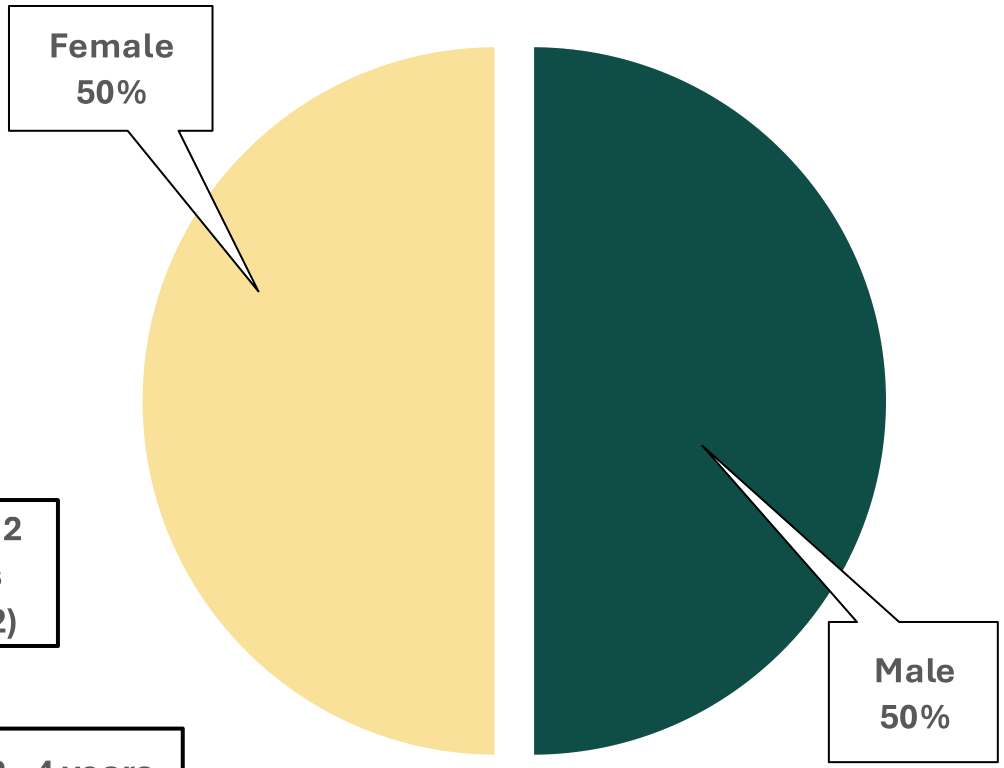
Participants

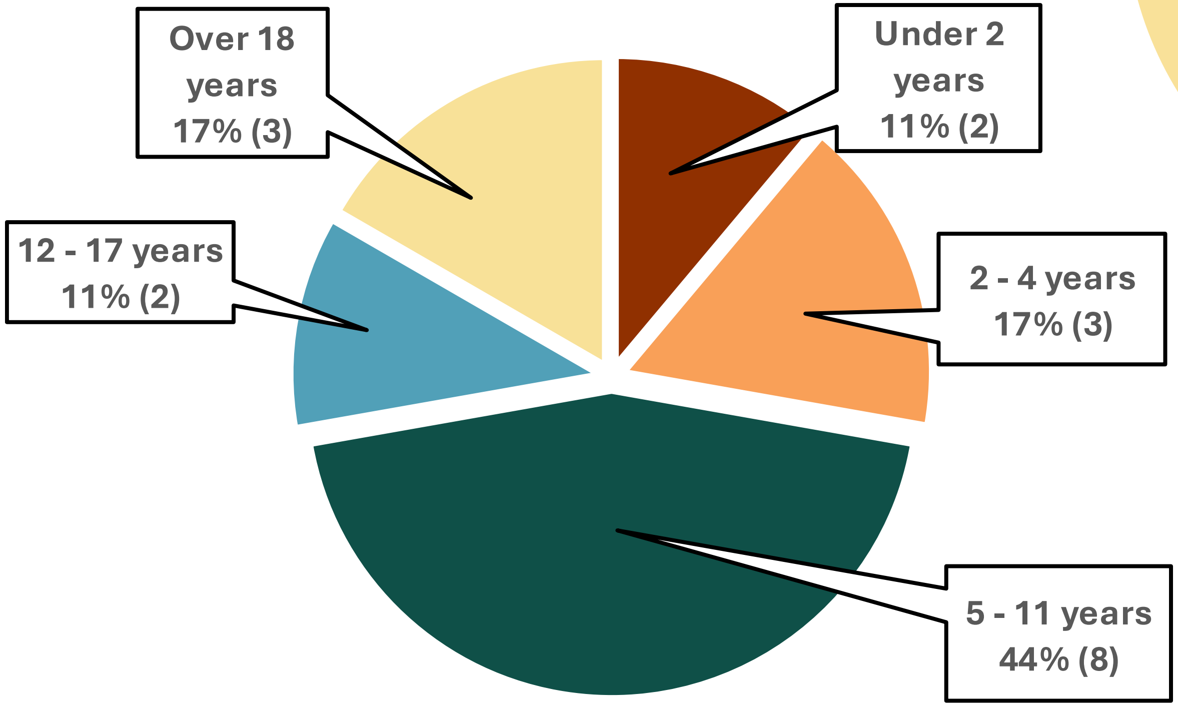
Individuals with SLC6A1 Represented by the Caregivers

- A total of 18:

  9 male

  9 female





Individual Age at the time of Interview

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Results

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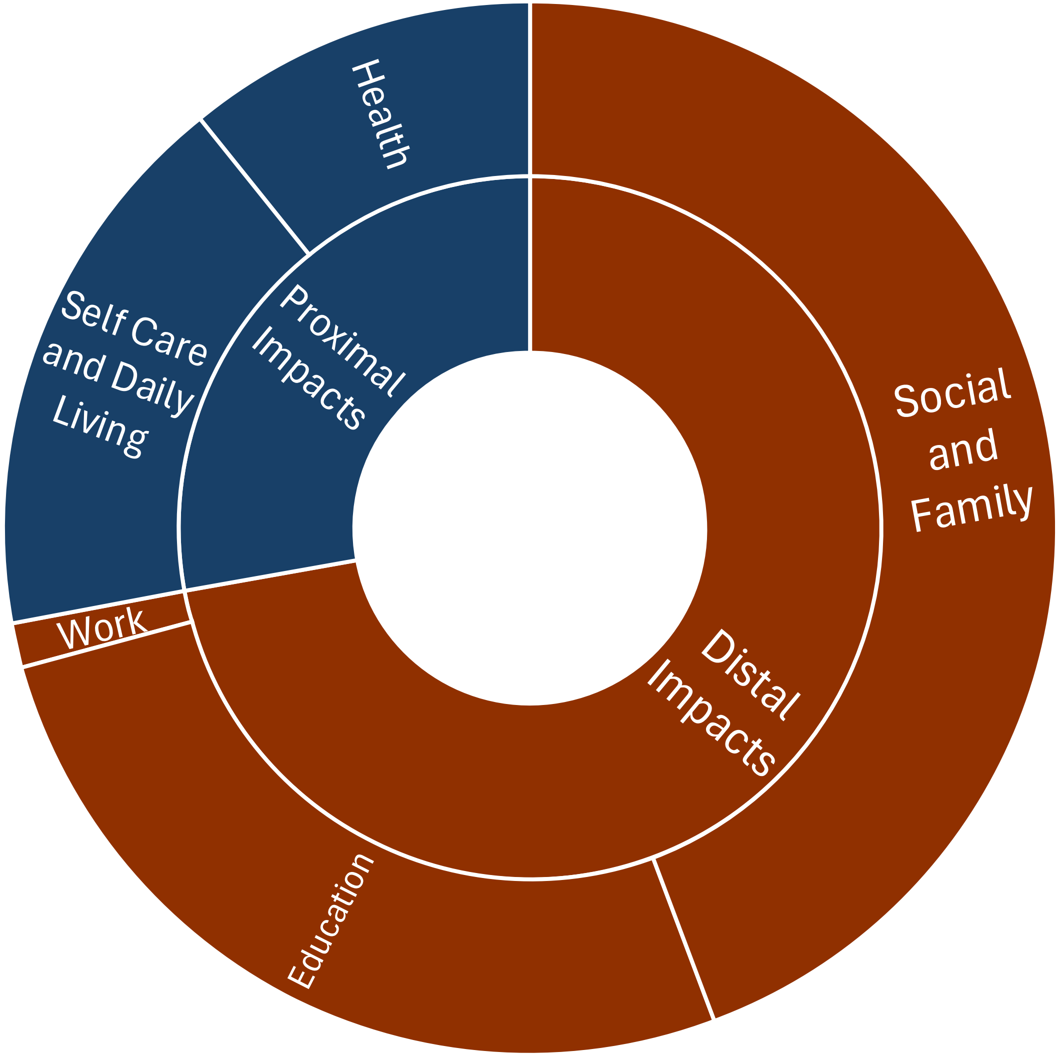
Caregiver Impacts

Individual Impacts



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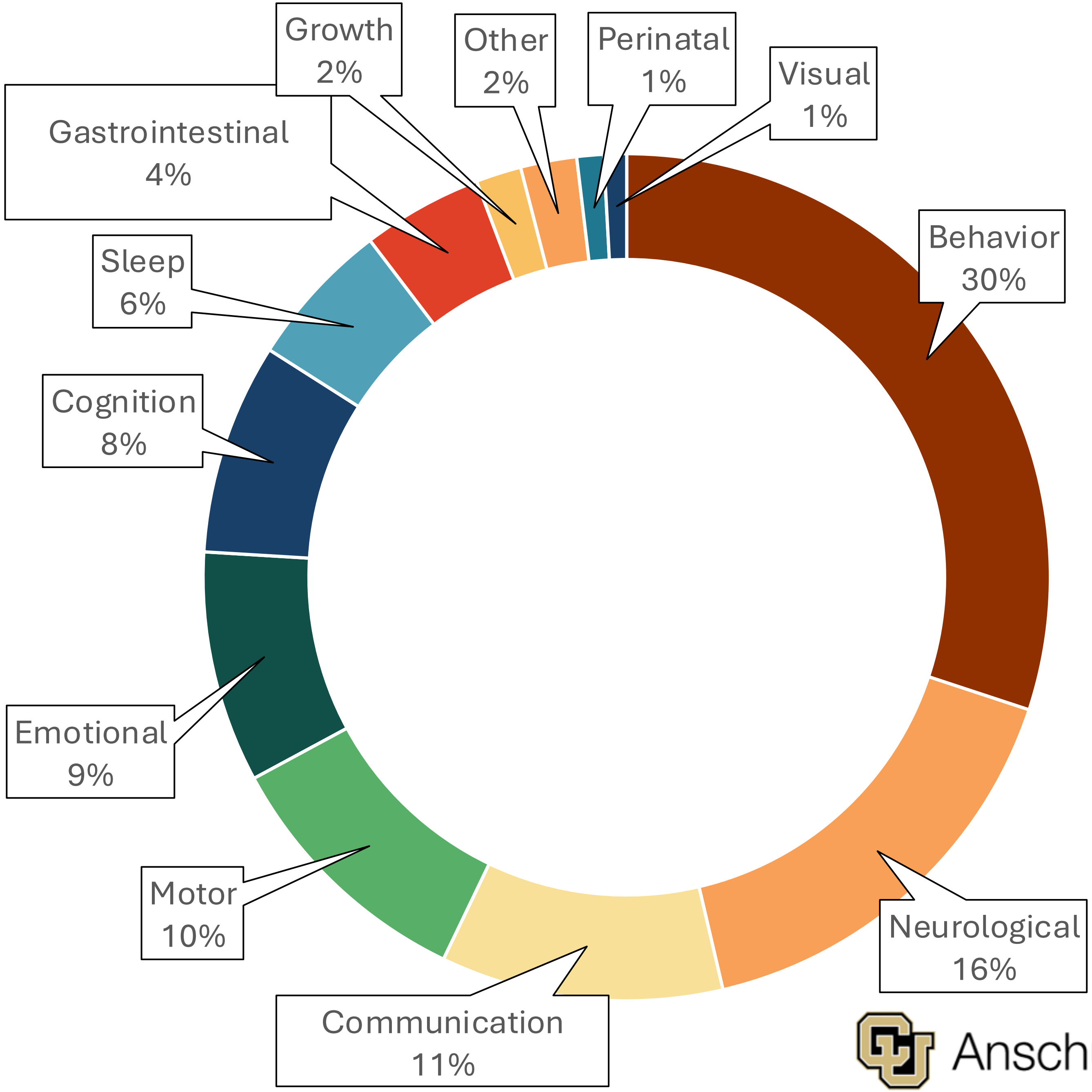
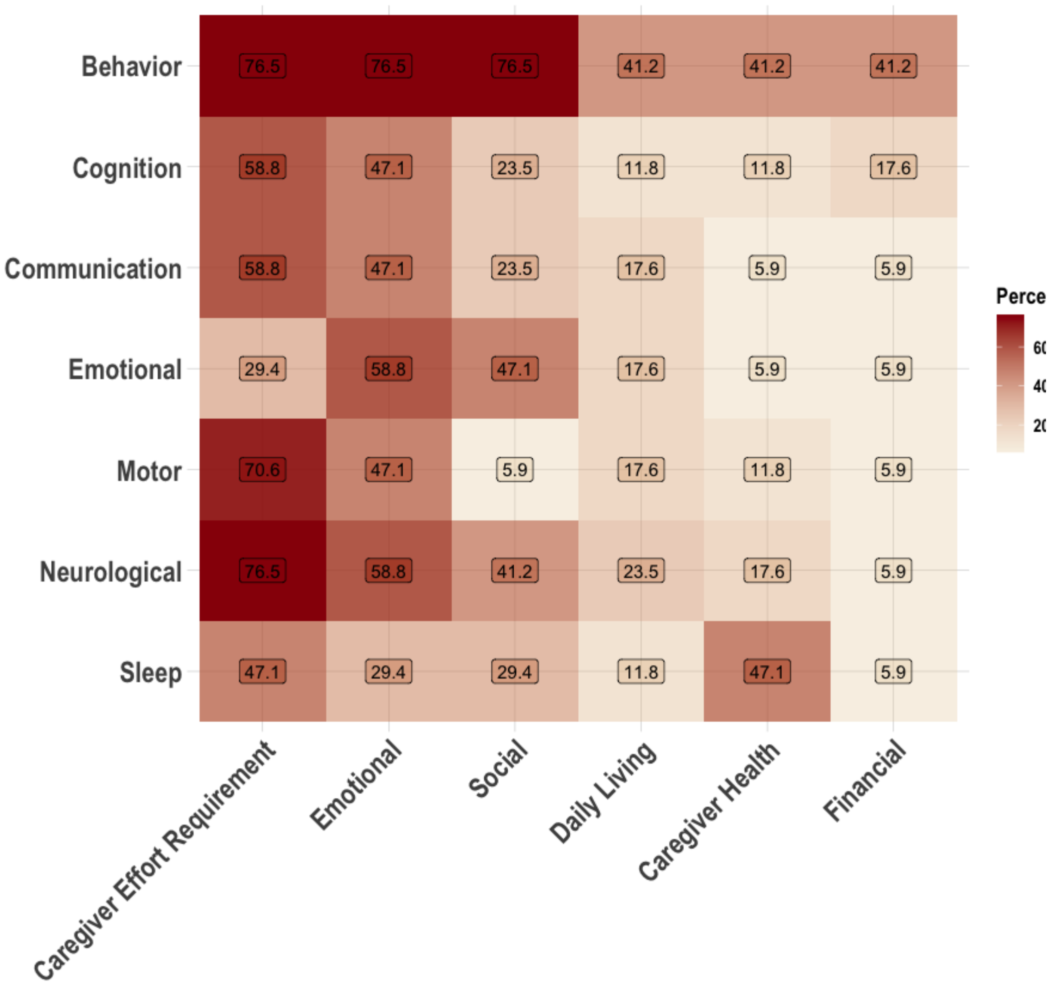
Major Symptom Domains

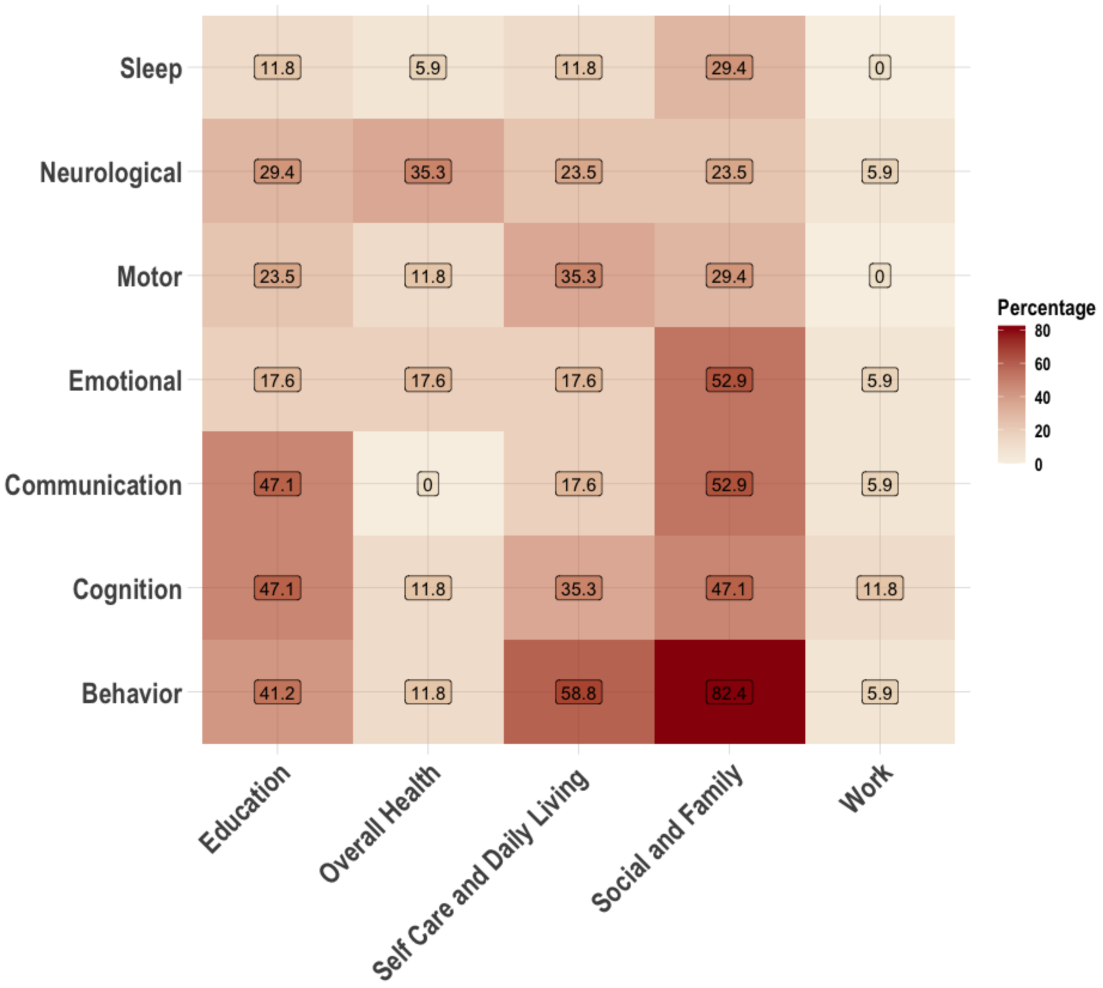


Symptom Domains and Caregiver Impacts Heatmap

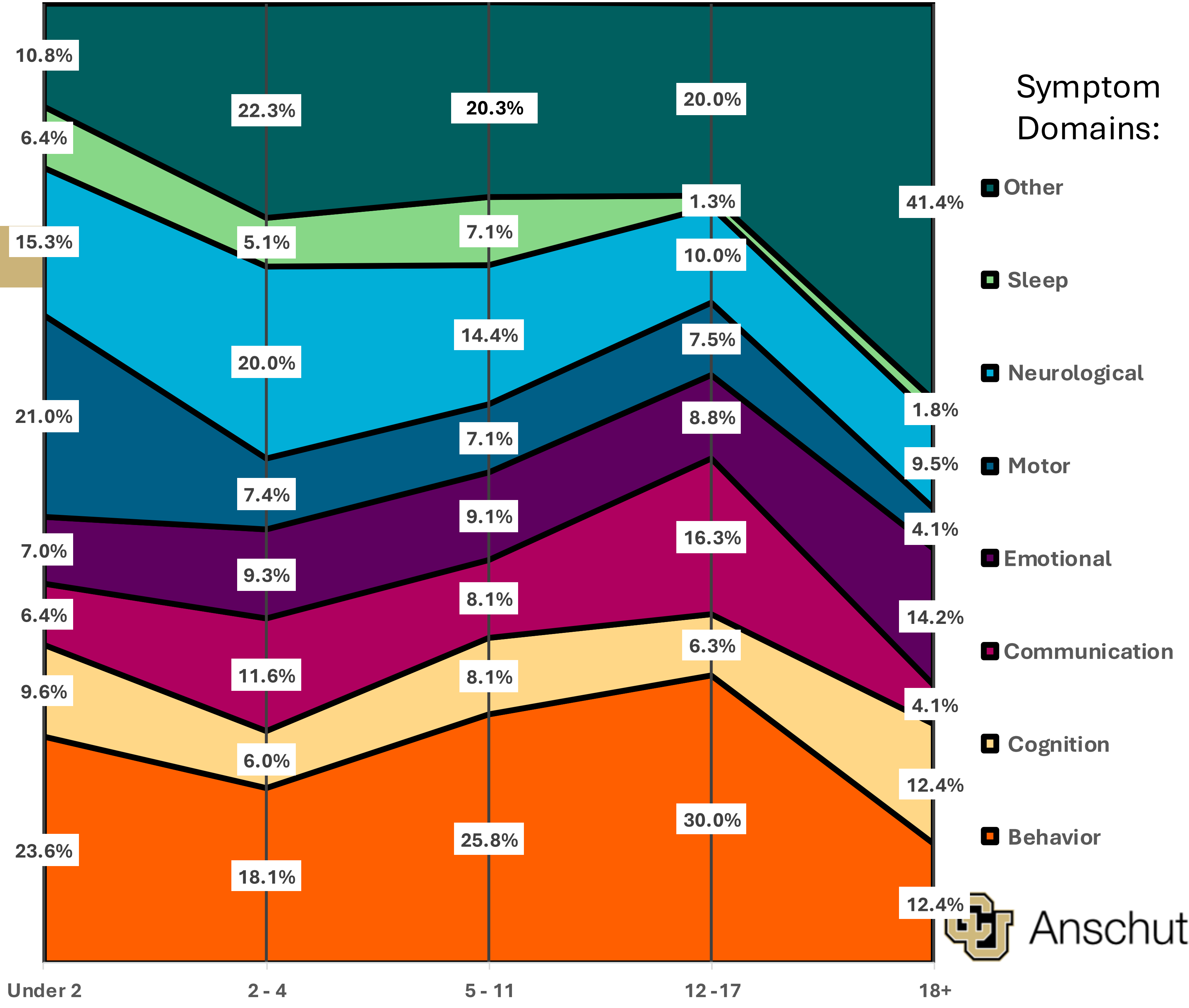
Caregiver Impact Heatmap



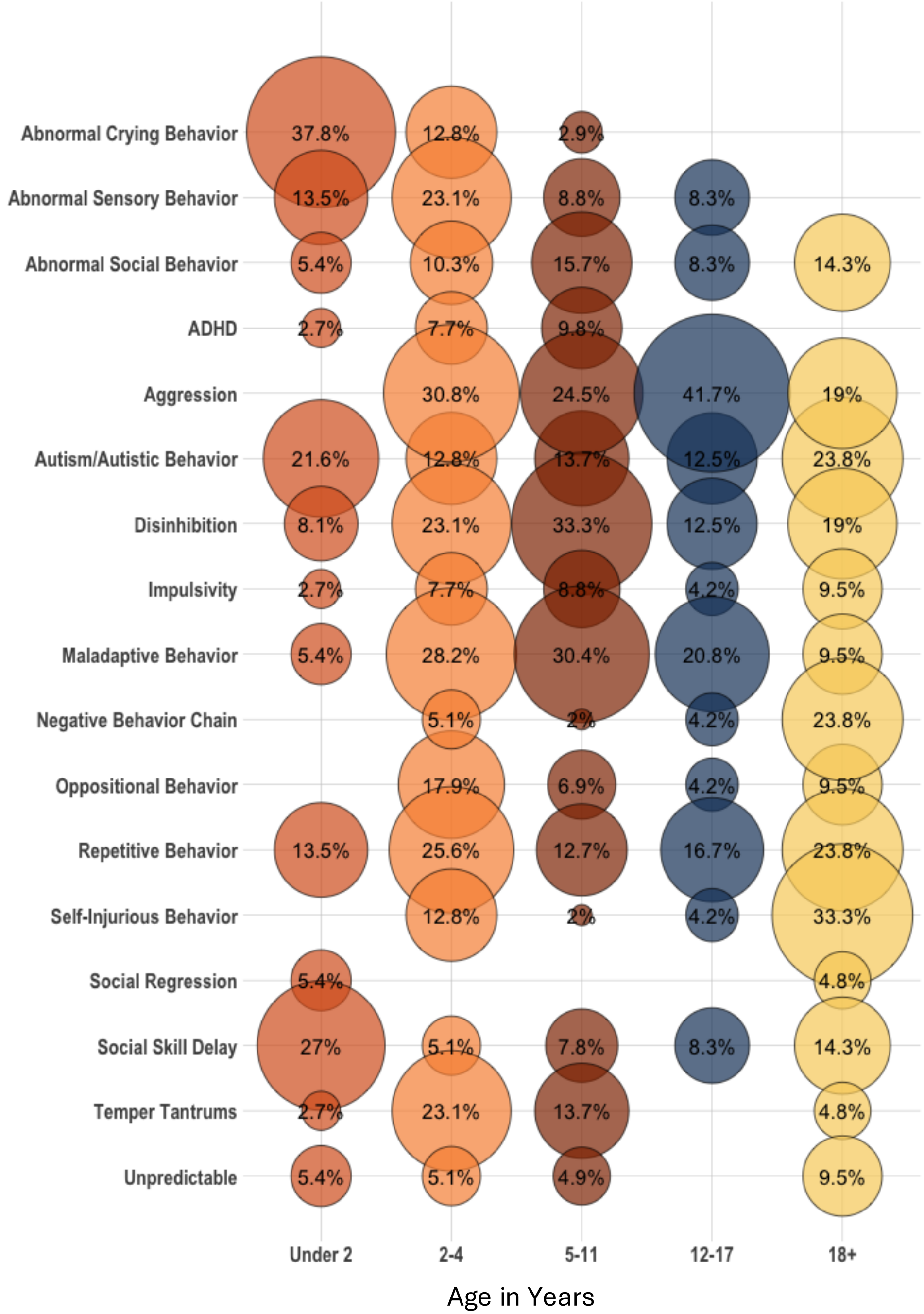
Individual Impact Heatmap



Symptom Domains Over Time



Behavior Subdomains Over Time



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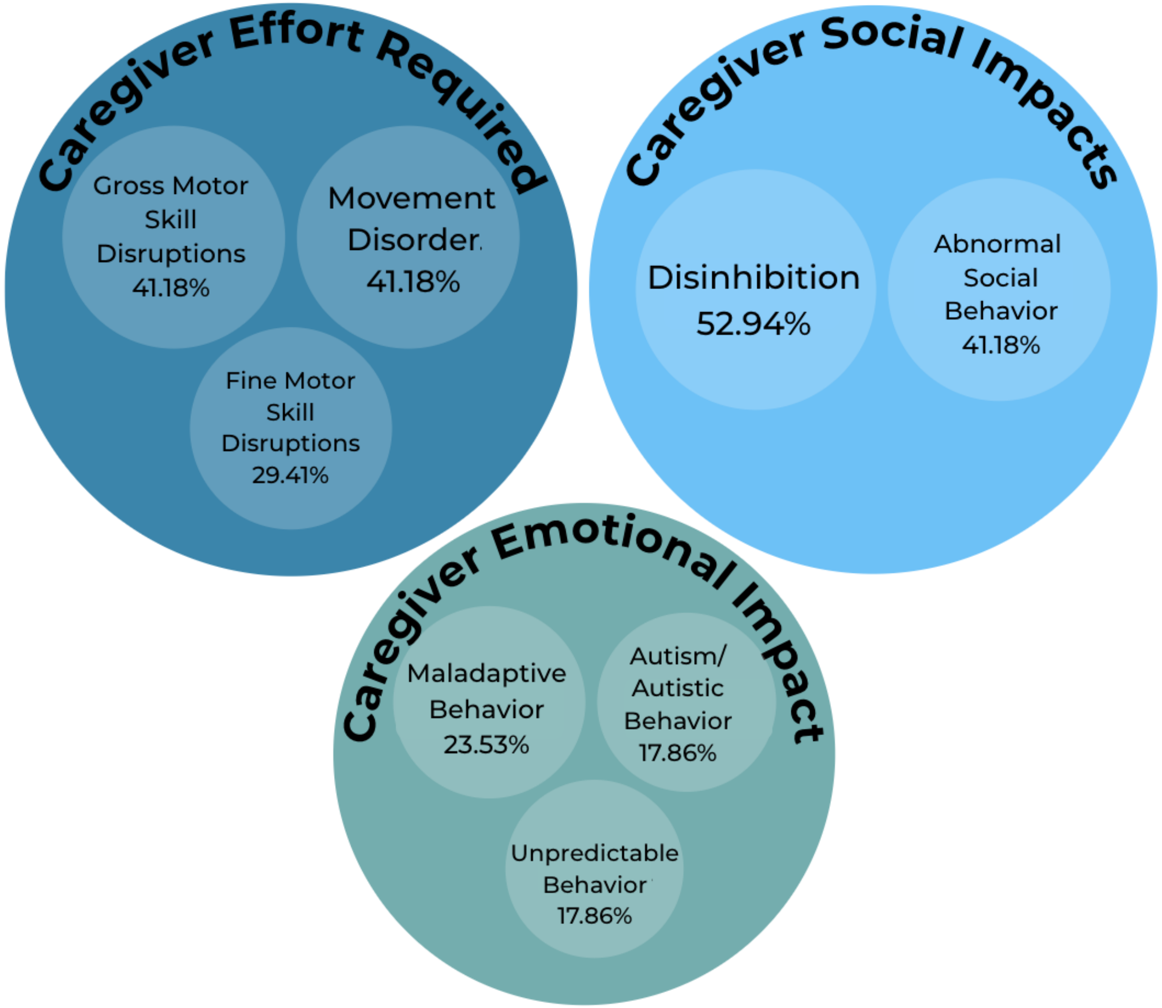
Selected Symptom Domain with Caregiver and Individual Impacts



Caregiver Effort Required

- Gross Motor Skill Disruptions 41.18%
- Movement Disorder 41.18%
- Fine Motor Skill Disruptions 29.41%

Caregiver Social Impacts

- Disinhibition 52.94%
- Abnormal Social Behavior 41.18%

Caregiver Emotional Impact

- Maladaptive Behavior 23.53%
- Autism/ Autistic Behavior 17.86%
- Unpredictable Behavior 17.86%

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Discussion

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- **Developing a DCM brings the caregivers and individuals most closely affected by a disorder into the research process.**
- **By doing this, we establish goals for natural history studies and clinical trials that most align with the lived experience.**
- **As targeted therapies are developed, this DCM will support the importance of behavior and emotional intervention across all ages.**
- **While seizures and other neurologic symptoms have great impacts, they cannot overshadow what caregivers have expressed to be the biggest barriers to education, socialization, sibling relationships, and caregiver health.**

Couldn’t have done it alone

- Sanjana Kalvakuntla
- Sara Poliquin
- Corinne Hunnicut
- Gary Heiman
- Sandra McEntee
- Haylie Romero
- Pamela McDonnell
- Lania Lusk
- Dallas Armstrong
- Kimberly Goodspeed
- Terri Jo Bichell an

SLC6A1 Connect
SLC6A1 Research & Support

COMBINED

You know, it's gotten better. It's not as bad as what it used to be, but it's a lot of running interference. You know we have to watch her all of that all the time. One of us… Somebody has to have eyes on her at all times. All times.

You just wanted to run away. And this went on from the time they got up till the time they went to bed and just all day long all day. You just wanted to run away.

It is what it is. But I wouldn't change it. I wouldn't change it. I wish I would. Well, I would change if I could be younger. That would help. Okay, I mean, we cry and we laugh, and when the kids go to bed we cuss, and you know we… we make it

And it seems like he would really want to have friends. He does want friends. Yeah. And like, he got in trouble at school this week because he wanted to play with somebody that didn't want to play with him. So he hit him and he just, thinks, Well, they won't play with me and so that's his response.

[After the diagnosis] we stopped caring about when milestones really occurred, it was more that the milestones were occurring. So like before that diagnosis, we were like, Oh my God, he is like so far behind… but after the diagnosis, it was like, OK. There are delayed like developments and like they can get better.

I would have never believed when she was younger, we'd be where we're at now.

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